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**PATENT**

Attorney Docket No. 34544/US/2

Dorsey File No. 459258-00048

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of:

GALLOP et al.

Serial No.: 10/766,990

Filing Date: January 28, 2004

For: *Amino Acid Derived Prodrugs of  
Propofol, Compositions and Uses  
Thereof*

Examiner: To Be Assigned

Art Unit: 1626

CERTIFICATE OF MAILING

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Signed: Careyna Fujimoto  
Careyna Fujimoto

**INFORMATION DISCLOSURE STATEMENT**

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Alexandria, VA 22313-1450

Sir:

In satisfaction of the duty of disclosure under 37 C.F.R. § 1.56, and in accordance with the provisions of 37 C.F.R. §§ 1.97 and 1.98, Applicants wish to draw the attention of the U.S. Patent and Trademark Office to the references cited on the accompanying form PTO/SB/08A-B. In accordance with 1287 Off. Gaz. Pat. Office 163, 10/19/2004, no copies of U.S. patents and U.S. published applications are enclosed. Copies of all other references are enclosed.

In accordance with the provision of 37 C.F.R. §§ 1.97(c)(1), and 1.97(e)(1), the undersigned certifies that references listed on the enclosed Form PTO/SB/08A-B, Substitute for Form PTO-1449, marked with an asterisk (\*), were first cited in a communication relating to the

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results of the international search report of Serial No. PCT/US04/02537, dated January 25, 2005, within three months prior to the filing of this Information Disclosure Statement. A copy of the International Search Report for the counterpart PCT application is enclosed herewith.

Nothing herein shall constitute an admission concerning the contents of any of the cited references, nor shall the inclusion of a reference herein be considered an admission that the reference constitutes prior art against the invention claimed in the above-identified application. Submission of the present document shall not be construed as an admission that a search has been made or that better art does not exist.

As far as is known to the undersigned, this Information Disclosure Statement is being filed within three months of the filing date of a national application, within three months of the date of entry of the national state in an international application, or before the mailing date of a first Office Action on the merits as set forth in 37 C.F.R. § 1.97(b), and therefore no fee is required.

While no further fee is believed to be due, if this belief is in error, the Commissioner is authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 50-2319 (File No. 459258-00048; Docket No. 34544/US/2/SKS).

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(415) 781-1989.



Dated: 3/30/05  
Dorsey & Whitney LLP  
Intellectual Property Department  
Four Embarcadero Center, Suite 3400  
San Francisco, CA 94111-4187  
Telephone: (415) 781-1989  
Facsimile: (415) 398-3249

Respectfully submitted,  
DORSEY & WHITNEY LLP

BY: Sunil K. Singh  
Sunil K. Singh, Reg. No. 45,298

Customer Number: 32940

Attachments:

Copy of International Search Report from Serial No. PCT/US04/02537 dated January 25, 2005  
Form PTO/SB/08A-B, Substitute for Form PTO-1449  
52 references

Substitute for form 1449A/PTO (Modified)  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)			<b>Complete if Known</b>		
			Application Number	10/766,990	
			Filing Date	January 28, 2004	
			First Named Inventor	Gallop, Mark A.	
			Art Unit	1626	
			Examiner Name	Not Assigned	
			Attorney Docket Number	34544/US/2/AMP/SKS (459258-00048)	
Sheet	1	of	4		

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. <sup>1</sup>	U.S. Patent Document Number-Kind Code <sup>2</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	A1	3,845,770	11-05-1974	Theeuwes et al.	
	A2	3,916,899	11-04-1975	Theeuwes et al.	
	A3	4,765,539	08-23-1988	Noakes et al.	
	A4	4,962,885	10-16-1990	Coffee	
	A5	5,112,598	05-12-1992	Biesalski	
	A6	5,556,611	09-17-1996	Biesalski	
	A7	5,698,155	12-16-1997	Grosswald et al.	
	A8	5,950,619	09-14-1999	van der Linden et al.	
	A9	5,954,047	09-21-1999	Armer et al.	
	A10	5,970, 974	10-26-1999	van der Linder et al.	
	A11 *	6,204,257 B1	03-20-2001	Stella et al.	
	A12 *	6,254,853 B1	07-03-2001	Hendler et al.	
	A13 *	6,362,234 B1	03-26-2002	Hendler	
	A14	6,451,776 B2	09-17-2002	Stella et al.	

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document Country Code <sup>2</sup> Number <sup>4</sup> Kind Code <sup>5</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
	B1	WO 94/12285 A2/A3	06-09-1994	Coffee		
	B2	WO 94/14543 A2/A3	07-07-19994	Coffee		
	B3	WO 95/26234 A1	10-05-1995	Coffee		
	B4	WO 95/26235 A1	10-05-1995	Coffee		
	B5	WO 95/32807 A1	12-07-1995	Coffee		
	B6	WO 99/58555 A2/A3	11-18-1999	Hendler et al.		
	B7 *	WO 00/48572 A1	08-24-2000	Morimoto et al.		
	B8	WO 00/54588 A1	09-21-2000	Krusz		
	B9	WO 02/13810 A1	02-21-2002	Hendler		

NON PATENT LITERATURE DOCUMENTS			
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This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the complete application form to the USPTO. Time will vary depending on the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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Substitute for form 1449A/PTO  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)			<b>Complete if Known</b>		
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Sheet	2	of	4	Attorney Docket Number	34544/US/2/AMP/SKS (459258-00048)

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	C1	Adibi, "The oligopeptide transporter (Pept-1) in Human Intestine: Biology and Function," <i>Gastroenterology</i> 1997, 113, 332-340.		
	C2	Alderman, "A Review of Cellulose Ethers in Hydrophilic Matrices <sup>of</sup> Oral controlled-Release Dosage Forms," <i>Int. J. Pharm. Tech. &amp; Prod. Mfr.</i> 1984, 5(3) 1-9.		
	C3	Anderson et al., "Alpha-amino acid phenolic ester derivatives: novel water-soluble general anesthetic agents which allosterically modulate GABA(A) receptors," <i>J. Med. Chem.</i> 2001, 44, 3582-3591.		
	C4	Bamba et al., "Release Mechanisms in Gelforming Sustained Release Preparations," <i>Int. J. Pharm.</i> 1979, 2, 307.		
	C5	Banaszczyk et al., "Propofol Phosphate, a Water-Soluble Propofol Prodrug: In Vivo Evaluation," <i>Anesth. Analg.</i> 2002, 95, 1285-1292. <sup>Cap</sup>		
	C6	Borgeat et al., "Adjuvant propofol enables better control of nausea and emesis secondary to chemotherapy for breast cancer," <i>Can. J. Anaesth.</i> 1994, 41, 1117-1119.		
	C7	Borgeat et al., "Propofol improves patient comfort during cisplatin chemotherapy. A pilot study," <i>Oncology</i> 1993, 50, 456-459. <sup>Cap</sup>		
	C8	Briggs et al., "An adverse reaction to the administration of disopropofol (Diprivan)," <i>Anaesthesia</i> 1982, 37, 1099-1101.		
	C9	Brooker et al., "Propofol Maintenance to Reduce Postoperative Emesis in Thyroidectomy Patients: A Group Sequential Comparison with Isoflurane/Nitrous Oxide," <i>Anaesth. Intensive Care</i> 1998, 26, 625-629		
	C10	Brown et al., "Role of Propofol in Refractory Status Epilepticus," <i>Pharmacother.</i> 1998, 32, 1053-1059.		
	C11	De la Cruz et al., "The Effect of Propofol on Oxidative Stress in Platelets from Surgical Patients," <i>Anesth. Analg.</i> 1999, 89, 1050-1055		
	C12	During et al., "Controlled release of dopamine from a polymeric brain implant: in vivo characterization," 1989, <i>Ann. Neurol.</i> 25:351.		
	C13	Gan et al., "Determination of Plasma Concentrations of Propofol Associated with 50% Reduction in Postoperative Nausea," <i>Anesthesiology</i> , 1997, 87, 779-784.		
	C14	Hasan et al., "Comparison of the Effects of the Propofol and Thiopental on the Pattern of Maximal Electroshock Seizures in a Rat," <i>Pharmacol. Toxicol.</i> 1994, 74, 50-53. <sup>Cap</sup>		
	C15	Holtkamp et al., "Propofol in subanesthetic doses terminates status epilepticus in a rodent model," <i>Ann. Neurol.</i> 2001, 49, 260-263. <sup>Cap</sup>		
	C16	Howard et al., "Intercerebral Drug Delivery in Rats with Lesion-Induced Memory Deficits," 1989, <i>J. Neurosurg.</i> 71:105-112.		
	C17	Krusz et al., "Intravenous Propofol: Unique Effectiveness in Treating Intractable Migraine," <i>Headache</i> 2000, 40, 224-230. <sup>Cap</sup>		
	C18	Kuisma et al., Propofol in prehospital treatment of convulsive status epilepticus. <i>Epilepsia</i> 1995, 36, 1241-1243.		

Examiner Signature	Date Considered
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	C19	Langer et al., "Chemical and Physical Structure of Polymers as Carriers for Controlled Release of Bioactive Agents: A Review," <i>J Macromol. Sci. Rev. Macromol Chem.</i> 1983, 23:61. CAP		
	C20	Langley et al., "Propofol. A review of its pharmacodynamic and pharmacokinetic properties and use as an intravenous anaesthetic," <i>Drugs</i> 1988, 35, 334-372. CAP		
	C21	Leibach et al., "Peptide transporters in the intestine and the kidney," <i>Ann. Rev. Nutr.</i> 1996, 16, 99-119.		
	C22	Levy et al., "Inhibition of Calcification of Bioprosthetic Heart Valves by Local Controlled-Release Diphosphonate," <i>Science</i> 1985 228: 190-192.		
	C23	Murphy et al., "The Antioxidant Potential of Propofol (2,6-Diisopropylphenol)," <i>Br. J. Anaesth.</i> 1992, 68, 613-618.		
	C24	Peduto et al., "Biochemical and Electrophysiologic Evidence That Propofol Enhances GABAergic Transmission in the Rat Brain," <i>Anesthesiology</i> 1991, 75, 1000-1009.		
	C25	Phelps et al., "Propofol in Chemotherapy-Associated Nausea and Vomiting," <i>Ann. Pharmacother.</i> 1996, 30, 290-292.		
	C26	Picard et al., "Prevention of Pain on Injection with Propofol: A Quantitative Systematic Review," 2000, 90, 963-969.		
	C27	Pop et al., "Synthesis and Preliminary Pharmacological Evaluation of Some Chemical Delivery Systems of 2,6-Diisopropylphenol (Propofol)," <i>Med. Chem. Res.</i> 1992, 2, 16-21.		
	C28	Raleigh et al., "Pharmacokinetics of Isoflretinoin (ISO) in Rats Following Oral Dosing or Aerosol Inhalation," <i>British J. Cancer</i> , 1999, 80, Suppl. 2, 96.		
	C29	Raleigh et al., "Searching for the Link Between Hypoxia and Poor Prognoses in Human Tumors," <i>Proc. Amer. Assoc. Cancer Research Annual Meeting</i> , 1999, 40, 397..		
	C30	Raoof et al., "In Vivo Assessment of Intestinal Hepatic, and Pulmonary First Pass Metabolism of Propofol in the Rat," <i>Pharm. Res.</i> 1996, 13, 891-895		
	C31	Sagara et al., "Propofol Hemisuccinate Protects Neuronal Cells from Oxidative Injury," <i>J. Neurochem.</i> 1999, 73, 2524-2530.		
	C32	Saudek et al., "A Preliminary Trial of the Programmable Implantable Medication System for Insulin Delivery," <i>N. Engl. J. Med.</i> , 1989, 321: 574.		
	C33	Sefton, "Implantable Pumps," <i>CRC Crit Ref Biomed. Eng.</i> 1987, 14:201.		
	C34	Simonian et al., "Oxidative Stress in Neurodegenerative Diseases," <i>Pharmacol. Toxicol.</i> 1996, 36, 83-106.		
	C35	Sutherland et al., "Propofol and Seizures," <i>Anaesth. Intensive Care</i> 1994, 22, 733-737.		
	C36	Tomioka et al., "Propofol is Effective in Chemotherapy-Induced Nausea and Vomiting: A Case Report with Quantitative Analysis," <i>Anesth. Analg.</i> 1999, 89, 798-799.		

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	C37	Tramer <i>et al.</i> , "Propofol Anaesthesia and Postoperative Nausea and Vomiting Quantitative and Systemic Review of Randomized Controlled Studies," <i>Br. J. Anaesth.</i> 1997, 78, 247-255.	
	C38 *	Trapani <i>et al.</i> , "Propofol Analogues. Synthesis, Relationships Between Structure and Affinity for GABA <sub>A</sub> Receptors," <i>J. Med. Chem.</i> 1998, 41, 1846-1854.	
	C39	Trapani <i>et al.</i> , "Water-Soluble Salts of Aminoacid Esters of the Anesthetic Agent Propofol," <i>Int. J. Pharm.</i> 1998, 175, 195-204.	
	C40	Verma <i>et al.</i> , "Osmotically Controlled Oral Drug Delivery," <i>Drug Dev. Ind. Pharm.</i> , 2000, 26:695-708.	
	C41	Walder <i>et al.</i> , "Seizure-like phenomena and propofol," <i>Neurology</i> 2002, 58, 1327-1332	
	C42	Wang <i>et al.</i> "Propofol reduces infarct size and striatal dopamine accumulation following transient middle cerebral artery occlusion: a microdialysis study," <i>Eur. J. Pharmacol.</i> 2002, 452, 303-308	
	C43	Young <i>et al.</i> , "Propofol neuroprotection in a rat model of ischaemia reperfusion injury," <i>Eur. J. Anaesthesiol.</i> 1997, 14, 320-326. ~~~~~	

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